

TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| | | |
|---|---|---|
| Applicant's or agent's file reference C1-A0320Y2P | FOR FURTHER ACTION | See Form PCT/IPEA/416 |
| International application No. PCT/JP2004/018506 | International filing date (day/month/year) 10.12.2004 | Priority date (day/month/year) 12.12.2003 |
| International Patent Classification (IPC) or national classification and IPC C07K16/28, C12N15/11, C12N5/06, A61K39/395 | | |
| Applicant CHUGAI SEIYAKU KABUSHIKI KAISHA | | |

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|---|--------------|---|-----------|---------------------|--------------------------|------------|----------|-------------------------------------|-------------|--|-------------------------------------|------------|----------------------------|-------------------------------------|-----------|---|--------------------------|------------|-------------------------|--------------------------|-------------|--|--------------------------|--------------|---|
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> | | | | | | | | | | | | | | | | | | | | | | | | | |
| <p>4. This report contains indications relating to the following items:</p> <table border="0"> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> | | <input checked="" type="checkbox"/> | Box No. I | Basis of the report | <input type="checkbox"/> | Box No. II | Priority | <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. II | Priority | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VI | Certain documents cited | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application | | | | | | | | | | | | | | | | | | | | | | | |

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|---|-----------------------------------|
| Date of submission of the demand | Date of completion of this report |
| Name and mailing address of the IPEA/JP | Authorized officer |
| Facsimile No. | Telephone No. |

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/018506

Box No. I

Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following _____ which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
- ☐ publication of the international application (Rule 12.4)
- ☐ international preliminary examination (Rule 55.2 and/or 55.3)
2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
- ☒ the international application as originally filed/furnished
- ☐ the description:
- pages _____ as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☐ the claims:
- nos. _____ as originally filed/furnished
- nos.* _____ as amended (together with any statement) under Article 19
- nos.* _____ received by this Authority on _____
- nos.* _____ received by this Authority on _____
- ☐ the drawings:
- sheets _____ as originally filed/furnished
- sheets* _____ received by this Authority on _____
- sheets* _____ received by this Authority on _____
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages _____
- ☐ the claims, nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/018506

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 5-38

because:

☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 5-38

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/018506

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:
- ☐ restricted the claims.
 - ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ neither restricted the claims nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
- ☐ complied with.
 - ☒ not complied with for the following reasons:

The polynucleotides having a base sequence represented by SEQ ID NOS: 1 to 65 and the polypeptides expressed by said polynucleotides as set forth in claim 1 do not share a common chemical structure, and the only commonality between the inventions set forth in the SEQ ID NOS is that specificity is only expressed in lung cancer, stomach cancer, cancer of the colon or hepatic cancer tissue.

However, document 1 sets forth a gene which is specifically expressed in cancer of the colon and lung cancer (Table 2, Co column and Lu column).

In addition, document 2 sets forth a gene which is specifically expressed in cancer of the colon (Table 1).

In addition, document 3 sets forth a gene which is specifically expressed in hepatic cancer (Table 2).

(Continued in Supplemental Box)

4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-4

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/018506

| Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | |
|---|---|-----|-----|
| 1. Statement | | | |
| Novelty (N) | Claims | | YES |
| | Claims | 1-4 | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-4 | NO |
| Industrial applicability (IA) | Claims | 1-4 | YES |
| | Claims | | NO |
| 2. Citations and explanations (Rule 70.7) | <p>Document 1: WO 02/33072 A1 (Chugai Pharmaceutical Co., Ltd.)</p> <p>Document 2: WO 02/33073 A1 (Chugai Pharmaceutical Co., Ltd.)</p> <p>Claims 1 to 4</p> <p>The invention set forth in claims 1 to 4 lacks novelty in the light of the inventions set forth in documents 1 and 2.</p> <p>Documents 1 and 2 set forth single chain polypeptides having bonding activity to a TPO receptor having two heavy chain variable regions and two light chain variable regions arranged in the order heavy chain variable region, light chain variable region, heavy chain variable region and light chain variable region with the N-terminal side as a reference point, wherein the polypeptide is bonded by linkers, and amino acids 3 to 18 are preferable as linkers, and amino acid 15 is used (document 1, page 4, line 19 to page 5, line 20; page 9, line 26 to page 13; line 27; page 68; fig. 34, document 2, page 4, line 27 to page 6, line 24; page 15, line 2 to page 16, line 28; page 31; fig. 34).</p> <p>Therefore there is no discernible difference between</p> | | |

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/018506

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

the inventions set forth in documents 1 and 2 and the
inventions set forth in claims 1 to 4.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/018506

Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, Item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☐ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2004/018506

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Therefore being specifically expressed only in lung cancer, stomach cancer, cancer of the colon or hepatic cancer tissue cannot be described as a special technical feature within the meaning of PCT Rule 13.2.

Such being the case, the inventions according to the 65 SEQ ID NOS set forth in claims 1 to 27 are considered not as a group of inventions so linked as to form a single general inventive concept but as a group of inventions comprising 65 inventions respectively relating to 65 different polynucleotides and the polypeptides expressed by these polynucleotides.

Document 1: SCHEURLE D. et al., Cancer gene discovery using digital differential display, Cancer Res. (2000), Vol. 60, No. 15, pages 4037 to 4043

Document 2: Matthias P. A. E. et al., Expression of Metallothionein II in Intestinal Metaplasia, Dysplasia, and Gastric Cancer, Cancer Research (2000), Vol. 60, pages 1995 to 2001

Document 3: Xu X.R. et al., Insight into hepatocellular carcinogenesis at transcriptome level by comparing gene expression profiles of hepatocellular carcinoma with those of corresponding noncancerous liver, Proc. Natl. Acad. Sci. USA. (2001), Vol. 98, No. 26, pages 4037 to 4043